March 12, 1896.

Sir JOSEPH LISTER, Bart., President, in the Chair.

A List of the Presents received was laid on the table, and thanks ordered for them.

The Right Hon. Sir Richard Temple, a Member of Her Majesty's Most Honourable Privy Council, was balloted for and elected a Fellow of the Society.

The Croonian Lecture was delivered as follows:—

CROONIAN LECTURE.—"Observations on Isolated Nerve. Electrical Changes a Measure of Physico-chemical Change." By AUGUSTUS D. WALLER, M.D., F.R.S.

(Abstract.)

The present investigation arises from experiments undertaken to determine autographically the varying relations between the magnitude of electrical change and the magnitude of stimulation in nerve under various chemical conditions.*

The main principle upon which the inquiry is based is the proposition established (by du Bois-Reymond, and by Hermann in particular) to the effect that disturbed protoplasm is electro-negative to the normal. An accessory principle to which reference will also be made, is that upheld (by Hering in particular) to the effect that protoplasm in which disturbance has just ceased is electro-positive to the normal.

In accordance with the first principle, injured is electro-negative to normal protoplasm, and excited is electro-negative to resting protoplasm.

In accordance with the second principle, recently excited is electro-positive to normal protoplasm.

Nerve (the excised and still-living nerve of the frog) is, for the purpose of this inquiry, considered as a convenient strand of excitable yet hardly exhaustible protoplasm, giving off to the galvanometer a demarcation or injury current (Hermann) from a less disturbed portion (longitudinal surface L) to a more disturbed portion (transverse section T), which current, during disturbance of the whole

* 'Physicl. Soc. Proc.,' June, 1895.

nerve effected by weak tetanisation at the two exciting electrodes *e, e*, but principally affecting a less disturbed portion L, undergoes a negative variation (du Bois-Reymond), the magnitude of which is taken as the index to the magnitude of chemico-physical change aroused in the nerve under various chemical conditions.

Care is observed to avoid the ordinary fallacies, and to obtain a "negative variation" as far as possible clear of electrotonic effects. Action-currents (significant of physiological effects in nerve) are distinguished from physical effects by means of anæsthetics, CO_2,Et_2O,$CHCl_3$.*

The physiological state of the nerve is tested by tetanising currents of low and uniform intensity, of uniform duration ($7\frac{1}{2}$ and later 15 seconds), at uniform intervals (1 minute), in both directions. The series of negative variations or action currents led off to the galvanometer, gives a corresponding series of deflections which are registered on a slowly descending photographic plate.

The plan of procedure adopted throughout has been to take for a period a normal series of deflections, then to submit the nerve to the action of a reagent (without removal from the electrodes in the case of gases, but with such removal in the case of solutions), finally to take for a further period the series of increasing or decreasing or reversed deflections of the chemically modified nerve. Alterations of resistance were controlled by aid of a standard deflection of 0·001 volt let into the nerve and galvanometer circuit at beginning and end of experiment.

The results so far acquired may be considered under the following heads :—

1. The effects of anæsthetics, and of some gases.
2. The effects of several chemical substances in solution.
3. The effect of carbon dioxide.
4. Theoretical considerations.

1. *Anæsthetic vapours* were employed at the outset of these observations with a view of distinguishing between physiological and physical effects. Their action was subsequently studied in detail, more especially as regards the comparison between ether and chloroform (and other chloromethanes and chloroethanes) upon living matter as represented by nerve.†

Ether vapour (Et_2O; also EtCl, EtBr, and EtI) produces a more or less prolonged abolition followed by complete recovery of excitability.

Chloroform vapour ($CHCl_3$; also other chloromethanes and chloroethanes) produces still more prolonged and frequently final abolition.

* 'Physiol. Soc. Proc.,' February, 1896.

† 'Physiol. Soc. Proc.,' November, 1895.

Small quantities of ether and of chloroform vapour produce temporary augmentation of excitability.

CO_2 assists the anæsthetic and counteracts the toxic action of $CHCl_3$.

Oxygen, hydrogen, nitrogen, carbon monoxide, nitrous oxide cause little or no effect.

Methane produces augmentation, hydrocyanic acid abolition.

Carbon dioxide in small quantity causes primary augmentation, in large quantity primary abolition or diminution, followed by secondary augmentation.

2. *Action of Reagents Soluble in Normal Saline.*

The nerve is bathed for 1 minute in more or less dilute solutions (acids, alkalis, neutral salts) and replaced upon the electrodes.

Distilled water gradually abolishes excitability.

Dilute acid solutions, M/40 to M/10, cause primary augmentation, followed by gradual diminution.

Stronger acid solutions, M/10 to M/5, cause primary diminution and abolition.

The effect of an acid follows acidity rather than avidity, but is also specific.

Decinormal acetic, nitric, and sulphuric acids have approximately equal effects.

As compared with the action of N/10 HNO_3, or H_2SO_4, the action of oxalic acid is less marked, that of phosphoric acid much less marked; that of lactic acid, on the other hand, is more marked. Approximately equal effects are produced by N/10 nitric, N/5 phosphoric, and N/20 lactic.

Alkalis.—Caustic potash is far more active than caustic soda. Potassium salts are more active than sodium salts.

Neutral Salts.—With the view of ascertaining how far the action of a neutral salt depends upon its acid or its basic moiety, the following tabular comparison was effected,

NH_4Cl.	NH_4Br.	NH_4I.
NaCl.	NaBr.	NaI.
KCl.	KBr.	KI.

From which is concluded that the influence of the base predominates in a total action due to the entire molecule.

Many other salts have been tested, among which may be mentioned those of calcium and of mercury.

Calcium chloride in M/10 solution augments the electrical response, and antagonises potassium chloride, which diminishes or abolishes it.

Mercuric chloride is the most lethal of any salts hitherto tested; its M/100 solution abolishes the response.

Isomeric compounds differ in efficacy.

Of the three dioxybenzenes, pyrocatechin is the most and hydroquinone the least toxic.

Alkaloids and Narcotic Drugs.—The most obviously effective, so far, have been cocaïne, physostigmine, and aconitine (chloral hydrate and butyl chloral hydrate); the most ineffective morphia, atropine, muscarine.

Extract of opium is more effective than tartrate of morphia.

Aconitine hydrochlorate is more effective than aconine, or pyraconitine, or pseudaconitine, or benzaconine; and there is a close resemblance between the effects of aconitine and of acetic acid, attributable to the acetyl group.

3. *Action of* CO_2 *on Nerve and Production of* CO_2 *by Nerve.*

Carbon dioxide, the chief terminal product of protoplasmic action, has been the object of detailed investigation, more especially with reference to the question of its production during the excited activity of nerve.*

A small amount of CO_2—such as is contained in *e.g.*, expired air—causes a marked augmentation of the negative variation. An isolated nerve acts thus as an indicator of the presence of CO_2.

From which it was argued that if any CO_2 is produced within the active (tetanised) nerve, a similar augmentation should occur. This has since been verified under various conditions.

The evidence is extended by further experiments on nerve in various stages, giving various kinds of electrical response to the same kind of excitation.

An isolated nerve (in autumn and early winter) considered with reference to its freshness presents three stages, in which the electrical response is as follows:—

I. A predominant negative effect.
II. " " positive after-effect.
III. " " " effect.

The effects of "little" CO_2, and of tetanisation lasting five minutes, upon nerve in these three states are as follows:—

I. Augmentation of negative deflection.
II. Appearance of negative deflection.
III. Substitution of negative for positive deflection, or diminution of positive deflection.

* 'Physiol. Soc Proc.,' January, 1896.

From which the conclusion is drawn that:—Tetanisation is attended with an evolution of CO_2 within the nerve.

4. *Theoretical Considerations.*

Phenomena of summation. Staircase phenomena. The possible nature of positive after-effects and of positive effects.

Phenomena associated with polarisation effects in nerve, and their modification by anæsthetics. Electrotonic currents and their negative variation. Polarising currents and their positive variation.

What is the possible mechanism of the positive and negative effects of the electrical excitation of medullated nerve?

What are the possible functional and chemical relations between the grey axis and the white sheath of a medullated fibre?

Presents, March 12, 1896.

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